Remarks

Rejection Under 35 U.S.C. § 102(b)

Claims 1-3 stand rejected under 35 U.S.C. § 102(b) over Suehiro.[1] Applicants respectfully traverse the rejection.

A reference cited under 35 U.S.C. § 102 must expressly or inherently describe each element set forth in the rejected claim. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). Independent claim 1 recites "determining SPHK1 gene copy number . . . . thereby generating data for a test gene copy number" and "comparing the test gene copy number to data for a control gene copy number . . . ." Suehiro does not expressly or inherently teach determining SPHK1 gene copy number or that amplification of an SPHK1 gene in a test sample relative to a control indicates the presence of a precancerous lesion or a cancer in a mammal. Suehiro therefore does not anticipate claims 1-3.

Please withdraw the rejection.

Rejection of Claims 1-3 Under 35 U.S.C. § 112 ¶ 2

Claims 1-3 stand rejected under 35 U.S.C. § 112 ¶ 2 as indefinite. The Office Action contends that the term "SPHK1 gene" does not provide any structural limitations for this aspect of the claim and that the specification does not provide a clear definition of "SPHK1." The Office Action also contends that the GenBank Accession Number for SPHK1 does not represent a fixed disclosure of a sequence. Applicants respectfully traverse the rejection.

Under 35 U.S.C. § 112, second paragraph, the claims must "reasonably apprise those skilled in the art both of the utilization and scope of the invention." *Georgia-Pacific Corp. v.*

[1] Suehiro *et al.*, "Genetic Aberrations Detected by Comparative Genomic Hybridization in Ovarian Clear Cell Adenocarcinomas," *Oncology 59*, 50-56, 2000.

United States Plywood Corp., 258 F.2d 124, 136, 118 U.S.P.Q. 122, 130 (2d Cir. 1958), *cert. denied*, 358 U.S. 884 (1958). Claims 1-3 serve this purpose. The specification teaches that the protein encoded by the naturally occurring SPHK1 gene is well known in the art:

> SPHK1 is a highly conserved lipid kinase that catalyzes the phosphorylation of sphingosine to form sphingosine-1-phosphate (S1P). SPHK1 is located on human chromosome 17q25.2. S1P and SPHK1 have been implicated in a signalling pathway that regulates diverse cellular functions, including cell growth, proliferation and survival. S1P is a lipid messenger with both intracellular and extracellular functions. Intracellularly, S1P regulates proliferation and survival, and extracellularly, it is a ligand for EDG family G-protein coupled receptors. It has been reported that SPHK1 gene can act as an oncogene (see, for example, WO 01/85953; Xia *et al.*, *Curr Biol.* 10(23):1527-30, 2000; Liu *et al.*, *Progress in Nucleic Acid Research and Molecular Biology* 71:493-511, 2002). It also has been reported that cells overexpressing SPHK1 can increase enzymatic activity and acquire a transformed phenotype, as determined by focus formation, colony growth in soft agar, and the ability to form tumours in nude mice (see Xia *et al.*, *Curr Biol.* 10(23): 1527-30, 2000). Several international and US publications describe aspects of SPHK1 gene and polypeptide (see for example, WO 01/31029, WO 00/55332, WO 00/70028, WO 01/53312, WO 00/52173, WO 01/60990, WO 99/12533, WO 99/61581, WO 98/54963, EP1074617, and U.S. Patent Application Publication No. 2002042358).

Page 7, lines 10-24. See also the following documents (copies are provided in the accompanying IDS):

- Ancellin *et al.*, "Extracellular Export of Sphingosine Kinase-1 Enzyme," *J. Biol. Chem. 277*, 6667-75, February 22, 2002;
- Doll *et al.*, "The epidermal growth factor stimulates sphingosine kinase-1 expression and activity in the human mammary carcinoma cell line MCF7," *Biochim. Biophys. Acta 1738*, 72-81, Epub December 27, 2005 (abstract);
- Edsall *et al.*, "Sphingosine kinase expression regulates apoptosis and caspases activation in PC12 cells," *J. Neurochem. 76*, 1573-84, March 2001 (abstract);

- Hayashi *et al.*, "Identification and Characterization of RPK118, a Novel Sphingosine Kinase-1-binding Protein," *J. Biol. Chem. 277*, 33319-24, September 6, 2002;

- Imamura *et al.*, "CpG island of rat sphingosine kinase-1 gene: tissue-dependent DNA methylation status and multiple alternative first exons," *Genomics 76*, 117-25, August 2001 (abstract);

- Johnson *et al.*, "PKC-dependent Activation of Sphingosine Kinase 1 and Translocation to the Plasma Membrane," *J. Biol. Chem. 277*, 35267-62, September 20, 2002;

- Lacaná *et al.*, "Cloning and Characterization of a Protein Kinase A Anchoring Protein (AKAP)-related Protein That Interacts with and Regulates Sphingosine Kinase 1 Activity," *J. Biol. Chem. 277*, 32947-63, September 6, 2002;

- Le Scolan *et al.*, "Overexpression of sphingosine kinase 1 is an oncogenic event in erythroleukemic progression," *Blood 106*, 1808-16, September 1, 2005, Epub May 12, 2005 (abstract);

- Liu *et al.*, "Molecular Cloning and Functional Characterization of a Novel Mammalian Sphingosine Kinase Type 2 Isoform," *J. Biol. Chem. 275*, 19513-20, June 30, 2000 (abstract);

- Melendez *et al.*, "Dichotomy of Ca2+ Signals Triggered by Different Phospholipid Pathways in Antigen Stimulation of Human Mast Cells," *J. Biol. Chem. 277*, 17255-62, May 10, 2002;

- Nakade *et al.*, "Regulation of sphingosine kinase 1 gene expression by protein kinase C in a human leukemia cell line, MEG-O1," *Biochim. Biophys. Acta 1635*, 104-16, December 30, 2003 (abstract);

- Nava *et al.*, "Functional characterization of human sphingosine kinase-1," *FEBS Lett. 473*, 81-84, May 4, 2000 (abstract);

- Pitson *et al.*, "A point mutant of human sphingosine kinase 1 with increased catalytic activity," *FEBS Lett. 509*, 169-73, December 7, 2001 (abstract);

- Pitson *et al.*, "The Nucleotide-binding Site of Human Sphingosine Kinase 1," *J. Biol. Chem. 277*, 49545-53, December 20, 2002;

- Sobue *et al.*, "Transcription factor specificity protein 1 (Sp1) is the main regulator of nerve growth factor-induced sphingosine kinase 1 gene expression of the rat pheochromocytoma cell line, PC12," *J. Neurochem. 95*, 940-49, November 2005, Epub August 31, 2005 (abstract);

- Taha *et al.*, "Loss of sphingosine kinase-1 activates the intrinsic pathway of programmed cell death: modulation of sphingolipid levels and the induction of apoptosis," *FASEB J. 20*, 482-84, March 2006, Epub December 30, 2005 (abstract);

- Van Brocklyn *et al.*, "Sphingosine kinase-1 expression correlates with poor survival of patients with glioblastoma multiforme: roles of sphingosine kinase isoforms in growth of glioblastoma cell lines," *J. Neuropathol. Exp. Neurol. 64*, 695-705, August 2005 (abstract); and

- Waters *et al.*, "Sphingosine 1-Phosphate and Platelet-derived Growth Factor (PDGF) Act via PDGFβ Receptor-Sphingosine 1-Phosphate Receptor Complexes in Airway Smooth Muscle Cells," *J. Biol. Chem. 278*, 6282-90, February 21, 2003.

Those skilled in the art readily understand what is encompassed by the term "SPHK1 gene." Claims 1-3 are therefore definite. Please withdraw the rejection.

Rejection Under 35 U.S.C. § 112 ¶ 1

Claims 1-3 stand rejected under 35 U.S.C. § 112 ¶ 1 as insufficiently described. The Office Action contends that the genus "SPHK1 gene" is too broad because the claims do not recite a structural limitation for the genus. Applicants respectfully traverse the rejection.

What is required to satisfy the written description requirement depends on the nature of the invention claimed. *In re DiLeone*, 436 F.2d 1404, 1405, 168 U.S.P.Q. 592, 593 (C.C.P.A. 1971). The methods of claims 1-3 requires determining SPHK1 gene copy number in a test sample obtained from a mammal; *i.e.*, the recited SPHK1 gene will be one which naturally occurs in the mammal. As the discussion above in connection with the rejection under 35 U.S.C. § 112 ¶ 2 demonstrates, the naturally occurring SPHK1 gene is well known in the art. An adequate written description of a gene which is well known in the art does not require a structural recitation either in the specification or in the claims. *See Capon v. Eshhar*, 418 F.3d

1349, 1360-61, 76 U.S.P.Q.2d 1078, 1087 (Fed. Cir. 2005) ("the Board erred in ruling that § 112 imposes a *per se* rule requiring recitation in the specification of the nucleotide sequence of claimed DNA, when that sequence is already known in the field."). Those skilled in the art would readily recognize that Applicants invented the subject matter of claims 1-3. The written description requirement for these claims is therefore satisfied. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 U.S.P.Q.2d 1111, 1117 (Fed. Cir. 1991).

Please withdraw the rejection.

Respectfully submitted,
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